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(71) Applicant *(for all designated States except US)*: **ALCHEMIA PTY LTD** [AU/AU]; 3 Hi-Tech Court, Brisbane Technology Park, Eight Miles Plains, Queensland 4113 (AU).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MEUTERMANS, Wim** [BE/AU]; 293 Birdwood Terrace, Toowong, Queensland 4066 (AU). **LE THANH, Giang** [AU/AU]; 38 Tarrant Street, MT GRAVATT, Queensland 4122 (AU). **ABBENANTE, Giovani** [AU/AU]; 53 Pringles Road, Sampsonvale, Queensland 4520 (AU). **TOMETZKI, Gerald** [GB/AU]; 106 Hardgreaves Road, Manly West, Queensland 4179 (AU). **HALLIDAY, Judy** [AU/AU]; 9 Minno Street, Chapel Hill, Queensland 4069 (AU). **ZEUGG, Johannes** [IT/AU]; 43 Wassell Street, WYNNUM, Queensland 4178 (AU).

(74) Agent: **CULLEN & CO.**; Level 26, 239 George Street, BRISBANE, Queensland 4000 (AU).

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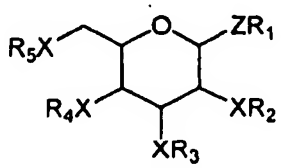
(54) Title: CLASSES OF COMPOUNDS THAT INTERACT WITH GPCRS



(I)

(57) Abstract: A method of inhibiting or effecting the activity of a GPCR which comprises contacting a GPCR with a compound of general formula (I), or a pharmaceutically acceptable salt thereof General Formula (I).

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CLASSES OF COMPOUNDS THAT INTERACT WITH GPCRs

FIELD OF THE INVENTION

The invention provides classes of biologically active compounds that interact in a pharmaceutically significant manner with G-Protein Coupled Receptors (GPCRs), pharmaceutical compositions containing such compounds and methods of treatment of humans suffering from a disorder which can be at least partially overcome by the compounds or compositions.

BACKGROUND OF THE INVENTION

The drug discovery landscape has been transformed by the genomics revolution. Advances in the understanding of biomolecular pathways and the roles they play in disease will lead to vast numbers of targets for therapeutic intervention. GPCRs represent the most important collection of therapeutic targets available.

GPCRs are proteins that tranduce signals across a cell membrane. They consist of a single polypeptide chain that threads back and forth seven times across the phospholipid bilayer that forms the cell membrane. The polypeptide chain has a portion inside the cell which form a G-protein coupling domain, and a receptor portion outside or in the cell wall. A signal molecule interacts with the receptor which sends the signal through the membrane wall and the signal causes the G-protein coupling domain to interact with a G protein.

Over 50% of marketed drugs target GPCRs. Whilst the druggable extent of GPCRs numbers some 450 receptors only some 200 GPCRs have been matched with their ligands. Orphan receptors suitable for drug targeting may therefore number in excess of 200 receptors. These are receptors with less than approximately 45% sequence identity to known GPCRs for which ligands have not been identified.

The targets of current GPCR drugs include, pain and inflammation, cancer, metabolic and gastrointestinal, cardiovascular and central nervous system disorders.

There is a continuing demand for new therapeutics, especially as our understanding of biological processes expands from the genomics revolution. The aforementioned GPCRs are suitable targets for therapeutic intervention due to their roles in such disorders as cancers, obesity and erectile dysfunction.

Considering the rate of generation and nature of the targets currently

being deconvoluted by biologists, there is a need for the development of drug candidates, designed in a rational manner to purposely interact with selected targets, such as the GPCRs.

From a drug discovery perspective, carbohydrate pyranose and furanose rings and their derivatives are well suited as templates. Each sugar represents a three-dimensional scaffold to which a variety of substituents can be attached, usually *via* a scaffold hydroxyl group, although occasionally a scaffold carboxyl or amino group may be present for substitution. By varying the substituents, their relative position on the sugar scaffold, and the type of sugar to which the substituents are coupled, numerous highly diverse structures are obtainable.

An important feature to note with carbohydrates, is that molecular diversity is achieved not only in the type of substituents, but also in the three dimensional presentation. The different stereoisomers of carbohydrates that occur naturally, offer the inherent structural advantage of providing alternative presentation of substituents.

Employing a related methodology, Hirschmann *et al* (Hirschmann, R., et. al., *J. Am. Chem. Soc.*, 1992, *114*, 9217-9218, US 5,552,534, WO 97/28172, WO 95/11686) synthesised several compounds designed as somatostatin analogues and integrin binders. The methodology employed by Hirschmann relied on protracted, linear, non-combinatorial syntheses, employed exclusively non-aminated pyranoses, and did not exploit any epimerisation chemistry to allow greater access to structural diversity. Consequently, these compounds and methods are manifestly distinct from this present invention.

We have developed a system that allows the chemical synthesis of highly structurally and functionally diverse derivatised carbohydrate and tetrahydropyran structures, of both natural and unnatural origin. The diversity accessible is particularly augmented by the juxtaposition of both structural and functional aspects of the molecules.

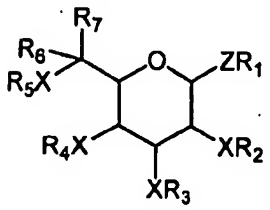
Using the axioms of this drug discovery methodology, we synthesised several novel classes of chemotypes in an effort to develop drug candidates against GPCR targets.

SUMMARY OF THE INVENTION

It is a general object of the invention to provide compounds that interact with GPCRs in a biologically significant manner,

It is an optional object of the invention to provide a pharmaceutical formulation comprising at least one compound as described herein or a pharmaceutically acceptable salt thereof, together with one or more pharmaceutically acceptable carriers, diluents or excipients.

In one aspect the invention provides for compounds of general formula I, that interact with GPCRs in a biologically significant manner,



General Formula I

Wherein the ring may be of any configuration;

Z is sulphur, oxygen, CH_2, C(O), C(O)HNR^A, NH, NR^A or hydrogen, in the case where Z is hydrogen then R_1 is not present, R^A is selected from the set defined for R_1 to R_5,

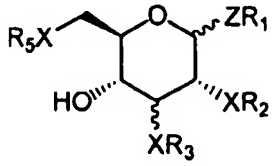
X is oxygen or nitrogen providing that at least one X of General Formula I is nitrogen, X may also combine independently with one of R_1 to R_5 to form an azide,

R_1 to R_5 are independently selected from the following definition which includes but is not limited to H or an alkyl, acyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl substituent of 1 to 20 atoms, which is optionally substituted, and can be branched or linear. Typical substituents include but are not limited to OH, NO, NO_2, NH_2, N_3, halogen, CF_3, CHF_2, CH_2F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramide, hydrazide, hydroxamate, hydroxamic acid,

heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl, which may optionally be further substituted, and

R_6 and R_7 are hydrogen, or may combine to form a carbonyl function.

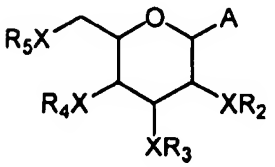
In one embodiment the invention provides for compounds of general formula II that interact with GPCRs in a biologically significant manner,



General Formula II

Wherein R_1, R_2, R_3, R_5, Z and X are defined as in General Formula I.

In a second embodiment the invention provides for compounds of general formula III that interact with GPCRs in a biologically significant manner,

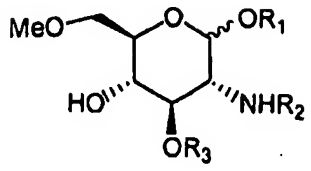


General Formula III

Wherein A is defined as hydrogen, SR_1, or OR_1 where R_1 is defined as in General Formula I, and

X and R_2 to R_5 are defined as in General Formula I.

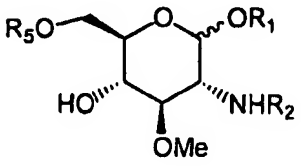
In a preferred embodiment the invention provides for compounds of General Formula IV that interact with GPCRs in a biologically significant manner,



General Formula IV

Wherein R_1-R_3 are defined as in General Formula I.

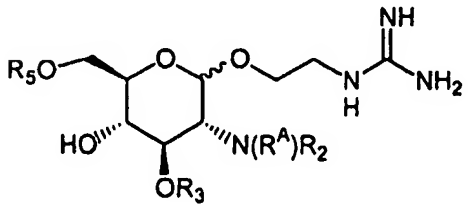
In a second preferred embodiment the invention provides for compounds of General Formula V that interact with GPCRs in a biologically significant manner,



General Formula V

Where in R_1, R_2 and R_5 are defined as in General Formula I.

In a third preferred embodiment the invention provides for compounds of General Formula VI that interact with GPCRs in a biologically significant manner,

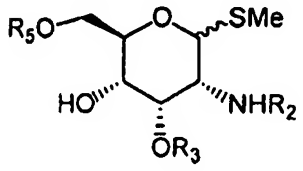


General Formula VI

Wherein R^A is H or combines with R_2 to form an azide, and

R_3, R_3 and R_5 are defined as in General Formula I.

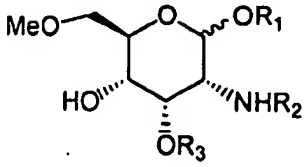
In a fourth preferred embodiment the invention provides for compounds General Formula VII that interact with GPCRs in a biologically significant manner of,



General Formula VII

Wherein, R_2, R_3 and R_5 are defined as in General Formula I.

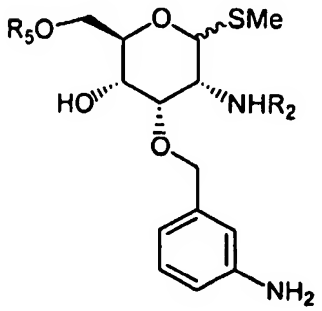
In a fifth preferred embodiment the invention provides for compounds of General Formula VIII that interact with GPCRs in a biologically significant manner,



General Formula VIII

Wherein R_1 to R_3 are defined as in General Formula I.

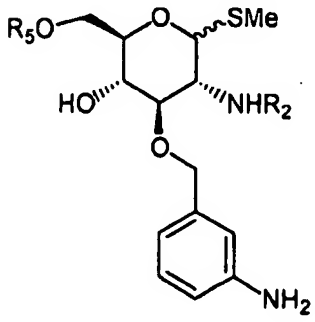
In a sixth preferred embodiment the invention provides for compounds of General Formula IX that interact with GPCRs in a biologically significant manner,



General Formula IX

Wherein R_2 and R_5 are defined as in General Formula I.

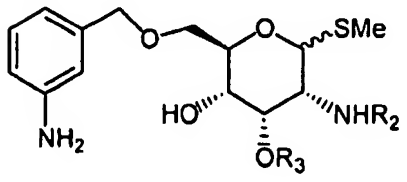
In a seventh preferred embodiment the invention provides for compounds of General Formula X that interact with GPCRs in a biologically significant manner,



General Formula X

Wherein R_2 and R_5 are defined as in General Formula I.

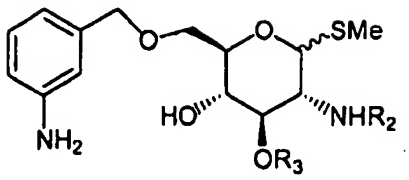
In an eighth preferred embodiment the invention provides for compounds of General Formula XI that interact with GPCRs in a biologically significant manner,



General Formula XI

Wherein R_2 and R_3 are defined as in General Formula I.

In a ninth preferred embodiment the invention provides for compounds of General Formula XII that interact with GPCRs in a biologically significant manner,



General Formula XII

Wherein R_2 and R_3 are defined as in General Formula I.

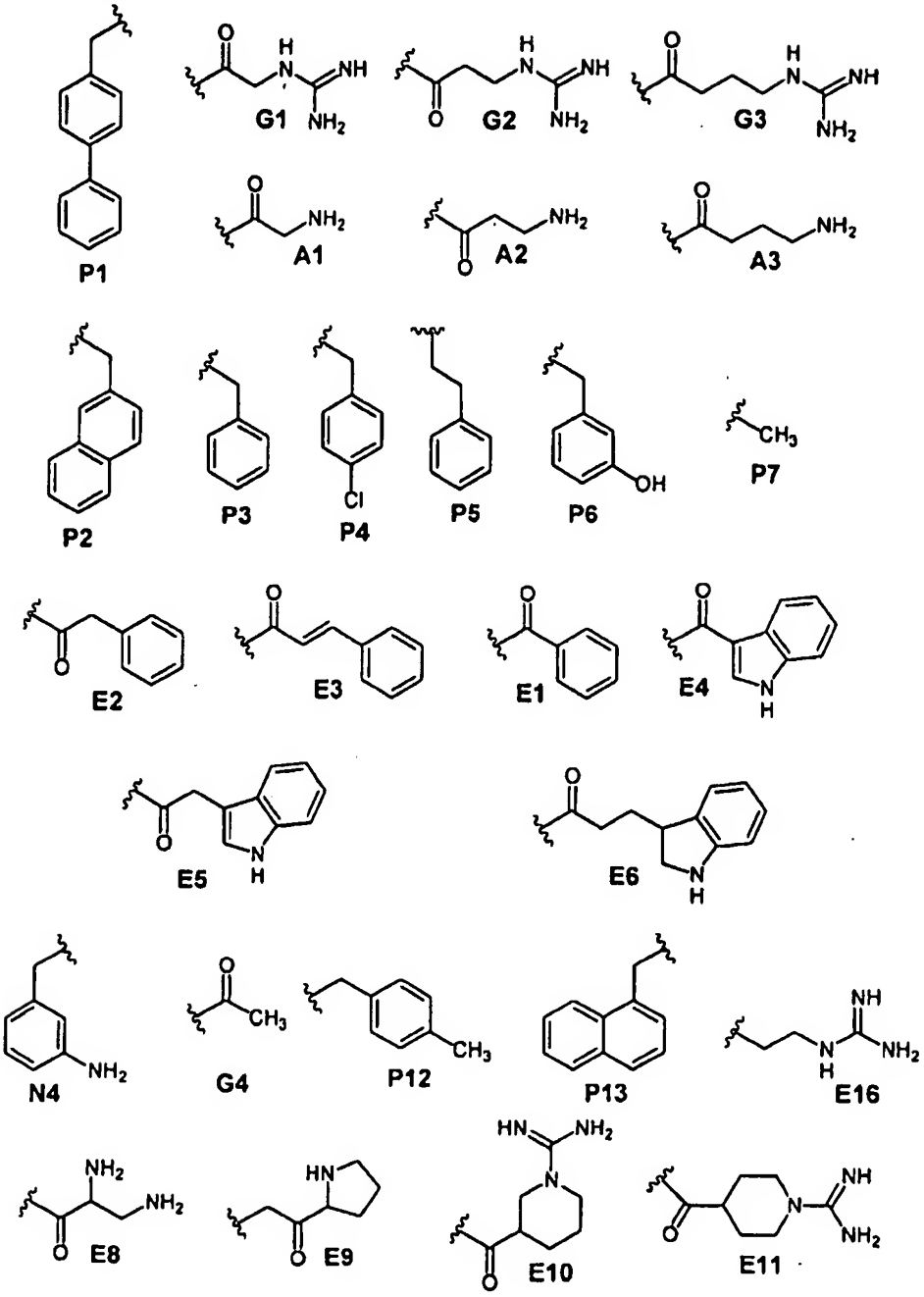
The compounds of the invention may be mixed with a pharmaceutical acceptable carrier, adjuvant, or vehicle which may comprise a-toxic carrier, adjuvant, or vehicle that may be administered to a patient, together with a compound of this invention, and which does not destroy the pharmacological activity thereof.

The pharmaceutical derivative may comprise a salt, ester, salt of an ester or other derivative of a compound of this invention which, upon administration to a recipient, is capable of providing, either directly or indirectly, a compound of this invention, although no limitation is meant thereby.

Compounds of the invention may be administered orally such as by means of a tabled, powder, liquid, emulsion, dispersion and the like; by inhalation; topically such as by means of a cream, ointment, salve etc; and as a suppository, although no limitation is meant thereby.

Examples of the Invention

Substituents per Example Libraries 1-14



5

Assay Conditions

GPCR radioligand binding (RLB) assays

Recombinant human receptors expressed in HEK 293 cells were used for all experiments. Receptor membrane preparations were purchased from Perkin Elmer BioSignal. The labelled ligand used in somatostatin GPCR RLB assays was [^{125}I]SST-14 and in melanocortin assays was [^{125}I]NDP-αMSH. All assays were done in a 96-well plate format using either glass fiber filter mats or filter plates. All reagents purchased were of the highest quality.

Specific assay buffer, incubation and washing conditions were optimized for each receptor however they all followed the same general format. The procedures for both filter mat and filter plate formats are based on the receptor manufacturers recommendations or those described extensively in the literature. The procedures are briefly outlined below.

In assays where filter mats are used we incubate receptor membranes, assay buffer and [^{125}I] labelled ligand in 96 well microplates. Add compounds to incubation mixture and continue incubation for optimized period. Presoak Filter mat GF/B in 0.5 % PEI for ~2 hr at 4°C. On completion of assay mixture incubation add additional 100µL/well of assay buffer immediately prior to filtration. Filter the assay mixture onto the GF/B filter mat using a cell harvester. Dry the filter mats prior to sealing them into a scintillation counting bag with scintillant. Radioactivity in each well is detected by liquid scintillation counting.

In assays where filter plates are used Multiscreen glass fiber filter plates (Millipore, Cat No MAFCNOB10) are precoated with 0.5 % PEI for ~2hr at 4°C. All wells are then washed with 200 □l/well assay buffer and filtered using the Multiscreen Separation System. Subsequently receptor membranes, assay buffer and labelled ligands are added to the wells and equilibrated. Compounds for testing are then added to the mixture and incubation is continued for an optimized time. Plates are then put into the Multiscreen Separation System and the assay mixture is filtered through the plate under vacuum. Each well is then washed several times with assay buffer. Plates are then dried prior to putting sealing tape onto the bottom of the plate. Scintillant is added to each well and radioactivity measured by liquid scintillation counting.

Comparison of assay conditions for 2 different assays

	MC4	SST5
	Volume □L	
Receptor membranes	20 (1:40 dilution of stock)	40 (1:40 dilution of stock)
labelled ligand (~80000 cpm)	10	40
unlabelled ligand	-	-
mQH_2O	-	-
Compounds	10	20
assay buffer	10	100
Total volume(□L)	50	200

Data analysis

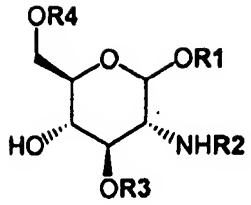
Raw data was analysed according to standard methods using either GraphPad Prism software or IDDBS ActivityBase software.

Key for Assay Results Libraries 1-14

"+" Indicates inhibition greater than...50%

"-" Indicates inhibition less than...50 %

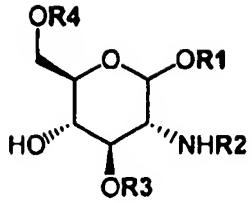
Example Library 1



Compound Number	R1	R2	R3	R4	MC4 inhibition at 10 micromolar	SST5 inhibition at 10 micromolar
1	P1	G1	P1	P7	+	+
2	P1	G2	P2	P7	-	+
3	P1	A3	P3	P7	-	+
4	P2	A3	P3	P7	-	+
5	P3	G1	P1	P7	+	-
6	P3	G2	P1	P7	+	+
7	P3	A3	P1	P7	-	+
8	P3	G3	P1	P7	-	+
9	P3	A3	P3	P7	-	+
10	P3	G2	P4	P7	-	+
11	P3	A3	P4	P7	-	+
12	P3	G3	P4	P7	-	+
13	P4	G2	P1	P7	+	+
14	P4	G2	P2	P7	+	+
15	P4	G3	P2	P7	+	+
16	P4	A3	P3	P7	-	+
17	P4	G2	P4	P7	-	+
18	P4	G3	P4	P7	-	+
19	P5	G1	P1	P7	+	-
20	P5	G2	P1	P7	+	-
21	P6	G2	P1	P7	-	+
22	P1	A3	P6	P7	-	+
23	P2	A3	P6	P7	-	+
24	P2	G3	P6	P7	-	+
25	P3	A3	P6	P7	-	+
26	P4	A3	P6	P7	-	+
27	P5	A3	P6	P7	-	+
28	P1	A3	P1	P7	+	+
29	P1	G3	P1	P7	+	+
30	P1	G3	P2	P7	+	+

31	P1	G2	P3	P7	-	+
32	P1	G2	P4	P7	+	+
33	P1	A3	P4	P7	+	+
34	P1	G3	P4	P7	+	+
35	P2	G1	P1	P7	+	+
36	P2	G2	P1	P7	+	+
37	P2	A3	P1	P7	+	+
38	P2	G2	P2	P7	+	+
39	P2	A3	P2	P7	+	+
40	P2	G3	P2	P7	+	+
41	P2	G3	P3	P7	-	+
42	P2	A3	P4	P7	-	+
43	P2	G3	P4	P7	+	+
44	P4	A3	P1	P7	-	+
45	P4	G3	P1	P7	+	+
46	P4	A3	P2	P7	+	+
47	P4	G3	P3	P7	-	+
48	P5	A3	P1	P7	-	+
49	P5	G3	P1	P7	+	+
50	P5	A3	P2	P7	-	+
51	P5	A3	P4	P7	-	+
52	P5	G3	P4	P7	-	+
53	P1	A3	P1	P7	+	+
54	P3	A3	P2	P7	-	+
55	P4	A3	P4	P7	-	+

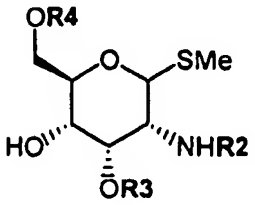
Example Library 2



Compound Number	R1	R2	R3	R4	MC4 Inhibition at 10 micromolar	SST5 Inhibition at 10 micromolar
56	P1	G1	P7	P1	+	+
57	P1	G2	P7	P1	+	+
58	P1	G3	P7	P1	+	-
59	P1	G1	P7	P2	+	-
60	P1	G2	P7	P2	-	+
61	P1	A3	P7	P2	+	+
62	P1	G3	P7	P2	+	-
63	P1	G1	P7	P4	+	-
64	P1	G2	P7	P4	+	-
65	P1	A3	P7	P4	+	-
66	P1	G3	P7	P4	+	-
67	P2	G1	P7	P1	+	-
68	P2	G2	P7	P1	+	-
69	P2	A3	P7	P1	+	+
70	P2	G3	P7	P1	+	-
71	P2	G1	P7	P2	+	-
72	P2	G2	P7	P2	+	-
73	P2	A3	P7	P2	+	+
74	P2	G3	P7	P2	+	-
75	P2	G1	P7	P4	+	-
76	P2	G2	P7	P4	+	-
77	P2	A3	P7	P4	+	+
78	P2	G3	P7	P4	+	-
79	P3	G3	P7	P1	+	-
80	P3	G1	P7	P2	+	+
81	P3	A3	P7	P4	-	+
82	P3	G3	P7	P4	+	-
83	P4	G1	P7	P1	+	-
84	P4	G2	P7	P1	+	+
85	P4	A3	P7	P1	-	+
86	P4	G3	P7	P1	+	+
87	P4	G1	P7	P2	+	+

88	P4	G2	P7	P2	+	+
89	P4	A3	P7	P2	+	+
90	P4	G3	P7	P2	+	+
91	P4	A3	P7	P3	-	+
92	P4	G1	P7	P4	+	-
93	P4	G2	P7	P4	+	-
94	P4	A3	P7	P4	+	+
95	P4	G3	P7	P4	+	-
96	P5	G1	P7	P1	+	-
97	P5	G2	P7	P1	+	-
98	P5	A3	P7	P1	+	+
99	P5	G3	P7	P1	+	-
100	P5	G1	P7	P2	+	-
101	P5	G2	P7	P2	+	-
102	P5	A3	P7	P2	+	+
103	P5	G3	P7	P2	+	+
104	P5	G1	P7	P4	+	-
105	P5	G2	P7	P4	+	-
106	P5	A3	P7	P4	+	+
107	P5	G3	P7	P4	+	-
108	P1	G1	P7	P6	+	-
109	P2	A3	P7	P6	-	+
110	P4	G2	P7	P6	+	-
111	P4	A3	P7	P6	-	+
112	P6	G1	P7	P1	+	-
113	P6	G2	P7	P1	+	-
114	P6	A3	P7	P1	+	-
115	P6	G3	P7	P2	+	-
116	P6	G2	P7	P2	+	-
117	P6	G3	P7	P2	+	-
118	P6	A3	P7	P4	-	+

Example Library 3

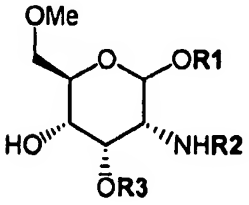


Compound Number	R2	R3	R4	MC4 inhibition at 10 micromolar	SST5 inhibition at 10 micromolar
119	A1	P3	P3	-	+
120	G1	P3	P3	+	+
121	A2	P3	P3	+	+
122	G2	P3	P3	+	+
123	A3	P3	P3	-	+
124	G3	P3	P3	+	+
125	A1	P3	P4	-	+
126	G1	P3	P4	+	+
127	A2	P3	P4	-	+
128	G2	P3	P4	+	+
129	A3	P3	P4	+	+
130	G3	P3	P4	+	+
131	A1	P3	P1	-	+
132	G1	P3	P1	+	+
133	A2	P3	P1	+	+
134	G2	P3	P1	+	+
135	A3	P3	P1	+	+
136	G3	P3	P1	+	+
137	A1	P3	P2	+	+
138	G1	P3	P2	+	+
139	A2	P3	P2	+	+
140	G2	P3	P2	+	+
141	A3	P3	P2	+	+
142	G3	P3	P2	+	+
143	A1	P4	P3	-	+
144	G1	P4	P3	+	+
145	A2	P4	P3	+	+
146	G2	P4	P3	+	+
147	A3	P4	P3	-	+
148	G3	P4	P3	+	+
149	A1	P4	P4	-	+
150	G1	P4	P4	+	+
151	A2	P4	P4	+	+

152	G2	P4	P4	+	+
153	A3	P4	P4	-	+
154	G3	P4	P4	+	+
155	A1	P4	P1	+	+
156	G1	P4	P1	+	+
157	A2	P4	P1	+	+
158	G2	P4	P1	+	+
159	A3	P4	P1	+	+
160	G3	P4	P1	+	+
161	A1	P4	P2	+	+
162	G1	P4	P2	+	+
163	A2	P4	P2	+	+
164	G2	P4	P2	+	+
165	A3	P4	P2	+	+
166	G3	P4	P2	+	+
167	A1	P1	P3	+	+
168	G1	P1	P3	+	+
169	A2	P1	P3	+	+
170	G2	P1	P3	+	+
171	A3	P1	P3	+	+
172	G3	P1	P3	+	+
173	A1	P1	P4	+	+
174	G1	P1	P4	+	+
175	A2	P1	P4	+	+
176	G2	P1	P4	+	+
177	A3	P1	P4	+	+
178	G3	P1	P4	+	+
179	A1	P1	P1	+	+
180	G1	P1	P1	+	+
181	A2	P1	P1	+	+
182	G2	P1	P1	+	+
183	A3	P1	P1	+	+
184	G3	P1	P1	-	+
185	A1	P1	P2	+	-
186	G1	P1	P2	+	+
187	A2	P1	P2	+	+
188	G2	P1	P2	+	+
189	A3	P1	P2	+	+
190	G3	P1	P2	+	+
191	A1	P2	P3	+	+
192	G1	P2	P3	+	+
193	A2	P2	P3	-	+
194	G2	P2	P3	+	+
195	A3	P2	P3	+	+
196	G3	P2	P3	+	+
197	A1	P2	P4	+	+

198	G1	P2	P4	+	+
199	A2	P2	P4	+	+
200	G2	P2	P4	+	+
201	A3	P2	P4	+	+
202	G3	P2	P4	+	+
203	A1	P2	P1	+	+
204	G1	P2	P1	+	+
205	A2	P2	P1	+	+
206	G2	P2	P1	+	+
207	A3	P2	P1	+	+
208	G3	P2	P1	+	+
209	A1	P2	P2	+	+
210	G1	P2	P2	+	+
211	A2	P2	P2	+	+
212	G2	P2	P2	+	+

Example Library 4

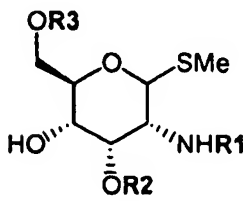


Compound Number	R1	R2	R3	MC4 inhibition at 10 micromolar	SST5 inhibition at 10 micromolar
213	P3	A1	P3	-	+
214	P3	G1	P3	+	+
215	P3	A2	P3	-	+
216	P3	G2	P3	+	+
217	P3	A3	P3	-	+
218	P3	G3	P3	+	+
219	P3	A1	P4	+	+
220	P3	G1	P4	+	+
221	P3	A2	P4	+	+
222	P3	G2	P4	+	+
223	P3	A3	P4	+	+
224	P3	G3	P4	+	+
225	P3	A1	P1	+	+
226	P3	G1	P1	+	+

227	P3	A2	P1	+	+
228	P3	G2	P1	+	+
229	P3	A3	P1	+	+
230	P3	G3	P1	+	+
231	P3	A1	P2	-	+
232	P3	G1	P2	+	+
233	P3	A2	P2	+	+
234	P3	G2	P2	+	+
235	P3	A3	P2	+	+
236	P3	G3	P2	+	+
237	P4	G1	P3	+	+
238	P4	A2	P3	-	+
239	P4	G2	P3	+	+
240	P4	A3	P3	-	+
241	P4	G3	P3	+	+
242	P4	A1	P4	+	+
243	P4	G1	P4	+	+
244	P4	A2	P4	+	+
245	P4	G2	P4	+	+
246	P4	A3	P4	+	+
247	P4	G3	P4	+	+
248	P4	A1	P1	+	+
249	P4	G1	P1	+	+
250	P4	A2	P1	+	+
251	P4	G2	P1	+	+
252	P4	A3	P1	+	+
253	P4	G3	P1	+	+
254	P4	A1	P2	+	+
255	P4	G1	P2	+	+
256	P4	A2	P2	+	+
257	P4	G2	P2	+	+
258	P4	A3	P2	+	+
259	P4	G3	P2	+	+
260	P5	A1	P3	-	+
261	P5	G1	P3	+	-
262	P5	A2	P3	-	+
263	P5	G2	P3	+	+
264	P5	A3	P3	-	+
265	P5	G3	P3	+	+
266	P5	A1	P4	-	+
267	P5	G1	P4	+	+
268	P5	A2	P4	+	+
269	P5	G2	P4	+	+
270	P5	A3	P4	+	+
271	P5	G3	P4	+	+
272	P5	A1	P1	+	+

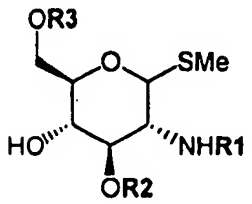
273	P5	G1	P1	+	+
274	P5	A2	P1	+	+
275	P5	G2	P1	+	+
276	P5	A3	P1	+	+
277	P5	G3	P1	+	+
278	P5	A1	P2	+	+
279	P5	G1	P2	+	+
280	P5	A2	P2	+	+
281	P5	G2	P2	+	+
282	P5	A3	P2	+	+
283	P5	G3	P2	+	+
284	P2	A1	P3	-	+
285	P2	G1	P3	+	+
286	P2	A2	P3	+	+
287	P2	G2	P3	+	+
288	P2	A3	P3	-	+
289	P2	G3	P3	-	+
290	P2	A1	P4	-	+
291	P2	G1	P4	+	+
292	P2	A2	P4	-	+
293	P2	G2	P4	+	+
294	P2	A3	P4	+	+
295	P2	G3	P4	+	+
296	P2	A1	P1	-	+
297	P2	G1	P1	+	+
298	P2	A2	P1	+	+
299	P2	G2	P1	+	+
300	P2	A3	P1	+	+
301	P2	G3	P1	+	+
302	P2	A1	P2	+	+
303	P2	G1	P2	+	+
304	P2	A2	P2	-	+
305	P2	G2	P2	+	+
306	P2	A3	P2	-	+
307	P2	G3	P2	+	+

Example Library 5



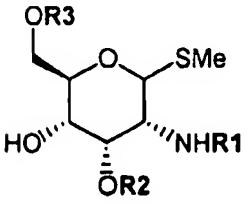
Compound Number	R1	R2	R3	MC4 inhibition at 10 micromolar	SST5 inhibition at 10 micromolar
308	P3	N4	E2	+	-
309	P3	N4	E4	+	-
310	P3	N4	E5	-	+
311	P3	N4	E6	+	+
312	P4	N4	E1	-	+
313	P4	N4	E2	+	+
314	P4	N4	E4	+	-
315	P4	N4	E5	-	+

Example Library 6



Compound Number	R1	R2	R3	MC4 inhibition at 10 micromolar	SST5 inhibition at 10 micromolar
316	E1	N4	P3	-	+
317	E2	N4	P3	+	-
318	E4	N4	P3	+	-
319	E5	N4	P3	-	+
320	E6	N4	P3	+	+
321	E1	N4	P4	-	+
322	E2	N4	P4	-	+
323	E4	N4	P4	+	-
324	E5	N4	P4	+	+
325	E6	N4	P4	+	-

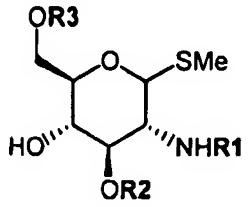
Example Library 7



Compound Number	R1	R2	R3	MC4 inhibition at 10 micromolar	SST5 inhibition at 10 micromolar
326	E1	P3	N4	-	+
327	E2	P3	N4	+	+
328	E4	P3	N4	+	-
329	E5	P3	N4	-	+
330	E6	P3	N4	+	+
331	E1	P4	N4	+	+

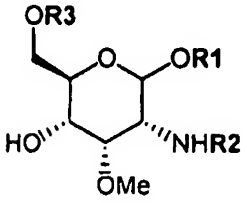
332	E6	P4	N4	+	-

Example Library 8



Compound Number	R1	R2	R3	MC4 inhibition at 10 micromolar	SST5 inhibition at 10 micromolar
333	E1	P3	N4	+	-
334	E2	P3	N4	+	-
335	E3	P3	N4	+	-
336	E5	P3	N4	+	+
337	E6	P3	N4	-	+
338	E1	P4	N4	+	+
339	E2	P4	N4	+	+
340	E3	P4	N4	+	-
341	E5	P4	N4	+	+

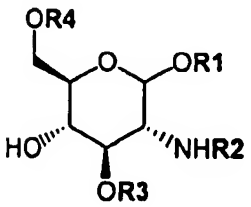
Example Library 9



Compound Number	R1	R2	R3	MC4 Inhibition at 4.0 Micromolar
342	P4	E8	P2	+
343	P4	E9	P2	+
344	P4	E10	P2	+

345	P4	G1	P2	+
346	P4	E8	P2	+
347	P4	E9	P2	+
348	P4	E11	P2	+
349	P4	G1	P2	+

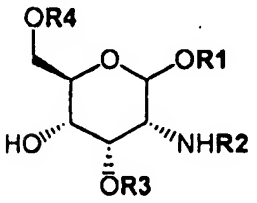
Example Library 10



Compound Number	R1	R2	R3	R4	MC4 Inhibition at 4.0 Micromolar
350	P2	A2	P4	P2	+
351	P2	A2	P4	P2	+
352	P2	A2	P4	P3	+
353	P2	A2	P4	P3	+
354	P2	A2	P4	P4	+
355	P2	A2	P4	P4	+
356	P2	A2	P2	P2	+
357	P2	A2	P2	P2	+
358	P2	A2	P2	P3	+
359	P2	A2	P2	P4	+
360	P2	A2	P2	P4	+
361	P2	A2	P3	P2	+
362	P2	A2	P3	P3	+
363	P2	A2	P3	P3	+
364	P2	A2	P3	P4	+
365	P2	A3	P4	P2	+
366	P2	A3	P4	P2	+
367	P2	A3	P4	P4	+
368	P2	A3	P4	P4	+
369	P2	A3	P2	P2	+
370	P2	A3	P2	P4	+
371	P2	A3	P2	P4	+
372	P2	A3	P3	P2	+
373	P2	A3	P3	P2	+

374	P2	A3	P3	P3	+
375	P2	A3	P3	P4	+
376	P4	A2	P4	P3	+
377	P4	A2	P4	P4	+
378	P4	A2	P2	P2	+
379	P4	A2	P2	P3	+
380	P4	A2	P2	P3	+
381	P4	A2	P2	P4	+
382	P4	A2	P2	P4	+
383	P4	A2	P3	P2	+
384	P4	A2	P3	P3	+
385	P4	A2	P3	P4	+
386	P4	A3	P4	P2	+
387	P4	A3	P4	P3	+
388	P4	A3	P4	P4	+
389	P4	A3	P2	P2	+
390	P4	A3	P2	P2	+
391	P4	A3	P2	P3	+
392	P4	A3	P2	P3	+
393	P4	A3	P2	P4	+
394	P4	A3	P2	P4	+
395	P4	A3	P3	P2	+
396	P4	A3	P3	P4	+

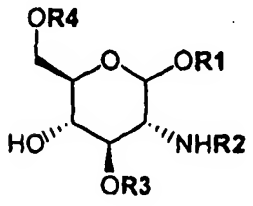
Example Library 11



Compound Number	R1	R2	R3	R4	MC4 Inhibition at 4.0 Micromolar
397	P3	A2	P4	P2	+
398	P3	A2	P4	P3	+
399	P3	A2	P4	P4	+
400	P3	A2	P2	P2	+
401	P3	A2	P2	P3	+
402	P3	A2	P2	P4	+

403	P3	A2	P3	P2	+
404	P3	A2	P3	P3	+
405	P3	A2	P3	P4	+
406	P3	A3	P4	P2	+
407	P3	A3	P4	P4	+
408	P3	A3	P2	P2	+
409	P3	A3	P2	P3	+
410	P3	A3	P2	P4	+
411	P3	A3	P3	P2	+
412	P3	A3	P3	P4	+
413	P2	A2	P4	P2	+
414	P2	A2	P4	P3	+
415	P2	A2	P4	P4	+
416	P2	A2	P2	P2	+
417	P2	A2	P2	P3	+
418	P2	A2	P2	P4	+
419	P2	A2	P3	P2	+
420	P2	A2	P3	P3	+
421	P2	A2	P3	P4	+
422	P2	A3	P4	P2	+
423	P2	A3	P4	P3	+
424	P2	A3	P4	P4	+
425	P2	A3	P2	P2	+
426	P2	A3	P2	P3	+
427	P2	A3	P2	P4	+
428	P2	A3	P3	P2	+
429	P2	A3	P3	P3	+
430	P2	A3	P3	P4	+

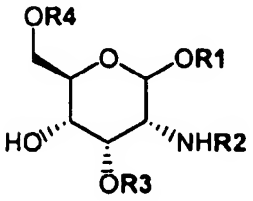
Example Library 12



Compound Number	R1	R2	R3	R4	MC4 Inhibition at 4.0 Micromolar
431	P3	G1	P4	P2	+

432	P3	G1	P4	P2	+
433	P3	G1	P4	P3	+
434	P3	G1	P4	P3	+
435	P3	G1	P4	P4	+
436	P3	G1	P2	P2	+
437	P3	G1	P2	P2	+
438	P3	G1	P2	P3	+
439	P3	G1	P2	P4	+
440	P3	G1	P2	P4	+
441	P3	G1	P1	P2	+
442	P3	G1	P1	P3	+
443	P3	G1	P1	P3	+
444	P3	G1	P1	P4	+
445	P3	G1	P1	P4	+
446	P3	G2	P4	P2	+
447	P3	G2	P4	P2	+
448	P3	G2	P4	P3	+
449	P3	G2	P4	P3	+
450	P3	G2	P4	P4	+
451	P3	G2	P4	P4	+
452	P3	G2	P2	P2	+
453	P3	G2	P2	P3	+
454	P3	G2	P2	P3	+
455	P3	G2	P2	P4	+
456	P3	G2	P2	P4	+
457	P3	G2	P1	P2	+
458	P3	G2	P1	P2	+
459	P3	G2	P1	P3	+
460	P3	G2	P1	P4	+
461	P3	G2	P1	P4	+
462	P3	G2	P1	P5	+

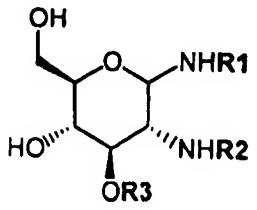
Example Library 13



Compound Number	R1	R2	R3	R4	MC4 Inhibition at 4.0

					Micromolar
463	P1	G1	P4	P2	+
464	P1	G1	P4	P3	+
465	P1	G1	P4	P4	+
466	P1	G1	P2	P3	+
467	P1	G1	P2	P4	+
468	P1	G1	P1	P3	+
469	P1	G1	P1	P4	+
470	P1	G2	P4	P2	+
471	P1	G2	P4	P3	+
472	P1	G2	P4	P4	+
473	P1	G2	P2	P2	+
474	P1	G2	P2	P3	+
475	P1	G2	P2	P4	+
476	P1	G2	P1	P2	+
477	P1	G2	P1	P3	+
478	P1	G2	P1	P4	+
479	P4	G1	P4	P2	+
480	P4	G1	P4	P3	+
481	P4	G1	P4	P4	+
482	P4	G1	P2	P2	+
483	P4	G1	P2	P3	+
484	P4	G1	P2	P4	+
485	P4	G1	P1	P2	+
486	P4	G1	P1	P3	+
487	P4	G1	P1	P4	+
488	P4	G2	P4	P2	+
489	P4	G2	P4	P3	+
490	P4	G2	P4	P4	+
491	P4	G2	P2	P2	+
492	P4	G2	P2	P3	+
493	P4	G2	P2	P4	+
494	P4	G2	P1	P2	+
495	P4	G2	P1	P3	+
496	P4	G2	P1	P4	+
497	P1	G3	P3	P3	+

Example Library 14

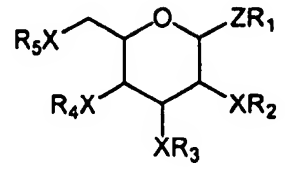


Compound Number	R1	R2	R3	MC4 Inhibition at 1.0 Micromolar
498	A2	G4	P3	+
499	A2	G4	P12	+
500	A2	G4	P13	+
501	A2	G4	P1	+
502	A2	E1	P3	+
503	A2	E1	P4	+
504	A2	E1	P12	+
505	A2	E1	P13	+
506	A1	E1	P3	+
507	A1	E1	P4	+

It should be appreciated that various other changes and modifications can be made to any embodiment described without departing from the spirit and scope of the invention.

CLAIMS:

1. A method of inhibiting or effecting the activity of a GPCR which comprises contacting a GPCR with a compound of general formula 1, or a pharmaceutically acceptable salt thereof



General Formula I

Wherein the ring may be of any configuration;

Z is selected from the group consisting of: sulphur, oxygen, or NR^A wherein R^A is selected from the set defined for R_1 to R_5 or C1 to C15 acyl, C4 to C15 arylacyl or C4 to C15 heteroarylacyl, with the proviso that both R_1 and R^A are not hydrogen,

X is selected from the group consisting of: oxygen or NR^A providing that at least one X of General Formula I is NR^A,

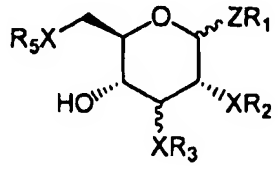
R_1 to R_5 are independently selected from the group consisting of: H, C1 to C12 alkyl, C1 to C12 alkenyl, C1 to C12 alkynyl, C1 to C12 heteroalkyl, C4 to C15 aryl, C4 to C15 heteroaryl, C4 to C15 arylalkyl or C4 to C15 heteroarylalkyl substituent ,

wherein, when X is NR^A, both R^A and the corresponding R_1 to R_5 are not hydrogen.

2. The method of claim 1, wherein any one of R^A or R_1 to R_5 is substituted with a moiety selected from the group consisting of: OH, NO, NO_2, NH_2, N_3, halogen, CF_3, CHF_2, CH_2F, nitrile, alkoxy, aryloxy, amidine, guanidiniums, carboxylic acid, carboxylic acid ester, carboxylic acid amide, aryl, cycloalkyl, heteroalkyl, heteroaryl, aminoalkyl, aminodialkyl, aminotrialkyl, aminoacyl, carbonyl, substituted or unsubstituted imine, sulfate, sulfonamide, phosphate, phosphoramide,

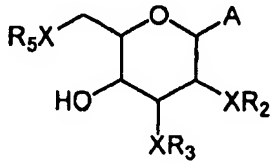
hydrazide, hydroxamate, hydroxamic acid, heteroaryloxy, aminoaryl, aminoheteroaryl, thioalkyl, thioaryl or thioheteroaryl.

3. The method of claim 1, wherein the compound is



General Formula II

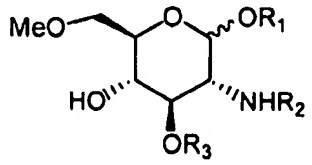
4. The method of claim 1, wherein the compound is



General Formula III

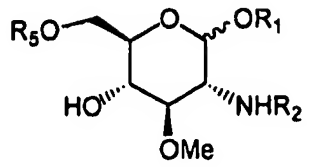
Wherein A is selected from the group consisting of: $N(R^A)R_1$, SR_1, or OR_1 .

5. The method of claim 1, wherein the compound is



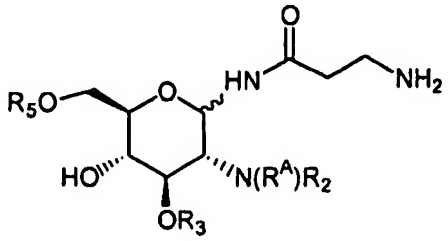
General Formula IV

6. The method of claim 1, wherein the compound is



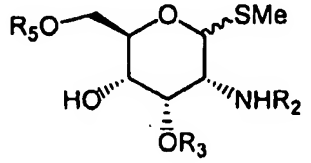
General Formula V

7. The method of claim 1, wherein the compound is



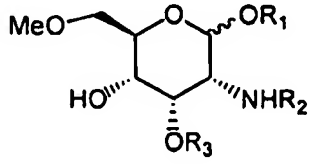
General Formula VI

8. The method of claim 1, wherein the compound is



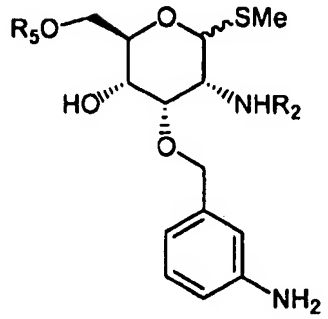
General Formula VII

9. The method of claim 1, wherein the compound is



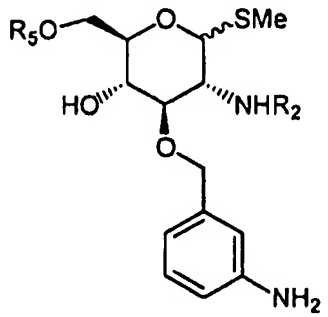
General Formula VIII

10. The method of claim 1, wherein the compound is



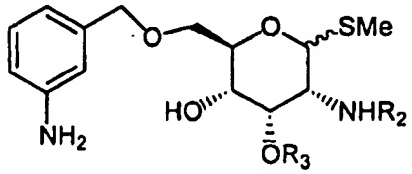
General Formula IX

11. The method of claim 1, wherein the compound is



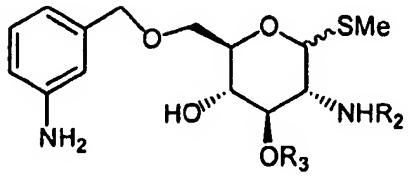
General Formula X

12. The method of claim 1, wherein the compound is



General Formula XI

13. The method of claim 1, wherein the compound is

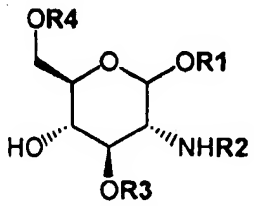


General Formula XII

14 The method of claim 1, wherein the receptor is a somatostatin receptor.

15. The method of claim 1, wherein the receptor is a melanocortin receptor.

16. The method of claim 14, wherein the compound is



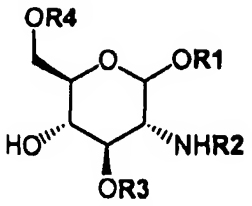
wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4
P1	G1	P1	P7
P1	G2	P2	P7
P1	A3	P3	P7
P2	A3	P3	P7
P3	G2	P1	P7
P3	A3	P1	P7
P3	G3	P1	P7
P3	A3	P3	P7
P3	G2	P4	P7
P3	A3	P4	P7
P3	G3	P4	P7
P4	G2	P1	P7
P4	G2	P2	P7
P4	G3	P2	P7
P4	A3	P3	P7

P4	G2	P4	P7
P4	G3	P4	P7
P6	G2	P1	P7
P1	A3	P6	P7
P2	A3	P6	P7
P2	G3	P6	P7
P3	A3	P6	P7
P4	A3	P6	P7
P5	A3	P6	P7
P1	A3	P1	P7
P1	G3	P1	P7
P1	G3	P2	P7
P1	G2	P3	P7
P1	G2	P4	P7
P1	A3	P4	P7
P1	G3	P4	P7
P2	G1	P1	P7
P2	G2	P1	P7
P2	A3	P1	P7
P2	G2	P2	P7
P2	A3	P2	P7
P2	G3	P2	P7
P2	G3	P3	P7
P2	A3	P4	P7
P2	G3	P4	P7
P4	A3	P1	P7
P4	G3	P1	P7
P4	A3	P2	P7
P4	G3	P3	P7
P5	A3	P1	P7
P5	G3	P1	P7
P5	A3	P2	P7
P5	A3	P4	P7
P5	G3	P4	P7
P1	A3	P1	P7
P3	A3	P2	P7
P4	A3	P4	P7

and wherein the groups A, P and G are as described in "Substituents per Example Libraries 1-14" in the specification.

17. The method of claim 15, wherein the compound is

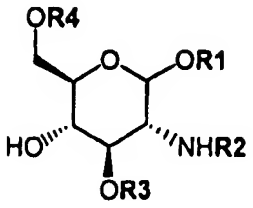


wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4	MC4 inhibition at 10 micromolar
P1	G1	P1	P7	+
P3	G1	P1	P7	+
P3	G2	P1	P7	+
P4	G2	P1	P7	+
P4	G2	P2	P7	+
P4	G3	P2	P7	+
P5	G1	P1	P7	+
P5	G2	P1	P7	+
P1	A3	P1	P7	+
P1	G3	P1	P7	+
P1	G3	P2	P7	+
P1	G2	P4	P7	+
P1	A3	P4	P7	+
P1	G3	P4	P7	+
P2	G1	P1	P7	+
P2	G2	P1	P7	+
P2	A3	P1	P7	+
P2	G2	P2	P7	+
P2	A3	P2	P7	+
P2	G3	P2	P7	+
P2	G3	P4	P7	+
P4	G3	P1	P7	+
P4	A3	P2	P7	+
P5	G3	P1	P7	+
P1	A3	P1	P7	+

and wherein the groups P, G and A are as described in "Substituents per Example Libraries 1-14" in the specification.

18. The method of claim 15, wherein the compound is



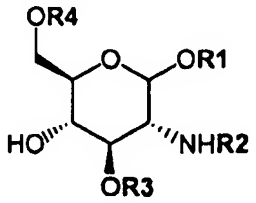
wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4
P1	G1	P7	P1
P1	G2	P7	P1
P1	G3	P7	P1
P1	G1	P7	P2
P1	A3	P7	P2
P1	G3	P7	P2
P1	G1	P7	P4
P1	G2	P7	P4
P1	A3	P7	P4
P1	G3	P7	P4
P2	G1	P7	P1
P2	G2	P7	P1
P2	A3	P7	P1
P2	G3	P7	P1
P2	G1	P7	P2
P2	G2	P7	P2
P2	A3	P7	P2
P2	G3	P7	P2
P2	G1	P7	P4
P2	G2	P7	P4
P2	A3	P7	P4
P2	G3	P7	P4
P3	G3	P7	P1
P3	G1	P7	P2
P3	G3	P7	P4
P4	G1	P7	P1
P4	G2	P7	P1
P4	G3	P7	P1
P4	G1	P7	P2
P4	G2	P7	P2
P4	A3	P7	P2
P4	G3	P7	P2
P4	G1	P7	P4
P4	G2	P7	P4

P4	A3	P7	P4
P4	G3	P7	P4
P5	G1	P7	P1
P5	G2	P7	P1
P5	A3	P7	P1
P5	G3	P7	P1
P5	G1	P7	P2
P5	G2	P7	P2
P5	A3	P7	P2
P5	G3	P7	P2
P5	G1	P7	P4
P5	G2	P7	P4
P5	A3	P7	P4
P5	G3	P7	P4
P1	G1	P7	P6
P4	G2	P7	P6
P6	G1	P7	P1
P6	G2	P7	P1
P6	A3	P7	P1
P6	G3	P7	P2
P6	G2	P7	P2
P6	G3	P7	P2

and wherein the groups P, G and A are as described in "Substituents per Example Libraries 1-14" in the specification.

19. The method of claim 14, wherein the compound is



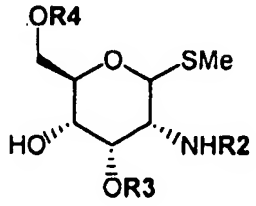
wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4
P1	G1	P7	P1
P1	G2	P7	P1
P1	G2	P7	P2
P1	A3	P7	P2
P2	A3	P7	P1
P2	A3	P7	P2
P2	A3	P7	P4

P3	G1	P7	P2
P3	A3	P7	P4
P4	G2	P7	P1
P4	A3	P7	P1
P4	G3	P7	P1
P4	G1	P7	P2
P4	G2	P7	P2
P4	A3	P7	P2
P4	G3	P7	P2
P4	A3	P7	P3
P4	A3	P7	P4
P5	A3	P7	P1
P5	A3	P7	P2
P5	G3	P7	P2
P5	A3	P7	P4
P2	A3	P7	P6
P4	A3	P7	P6
P6	A3	P7	P4

and wherein the groups P, G and A are as described in "Substituents per Example Libraries 1-14" in the specification.

20. The method of claim 15, wherein the compound is



wherein

R4, R2 and R3 are selected from the group combinations of :

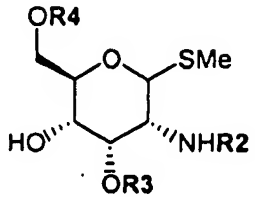
R2	R3	R4
G1	P3	P3
A2	P3	P3
G2	P3	P3
G3	P3	P3
G1	P3	P4
G2	P3	P4
A3	P3	P4
G3	P3	P4

G1	P3	P1
A2	P3	P1
G2	P3	P1
A3	P3	P1
G3	P3	P1
A1	P3	P2
G1	P3	P2
A2	P3	P2
G2	P3	P2
A3	P3	P2
G3	P3	P2
G1	P4	P3
A2	P4	P3
G2	P4	P3
G3	P4	P3
G1	P4	P4
A2	P4	P4
G2	P4	P4
G3	P4	P4
A1	P4	P1
G1	P4	P1
A2	P4	P1
G2	P4	P1
A3	P4	P1
G3	P4	P1
A1	P4	P2
G1	P4	P2
A2	P4	P2
G2	P4	P2
A3	P4	P2
G3	P4	P2
A1	P1	P3
G1	P1	P3
A2	P1	P3
G2	P1	P3
A3	P1	P3
G3	P1	P3
A1	P1	P4
G1	P1	P4
A2	P1	P4
G2	P1	P4
A3	P1	P4
G3	P1	P4
A1	P1	P1
G1	P1	P1
A2	P1	P1

G2	P1	P1
A3	P1	P1
A1	P1	P2
G1	P1	P2
A2	P1	P2
G2	P1	P2
A3	P1	P2
G3	P1	P2
A1	P2	P3
G1	P2	P3
G2	P2	P3
A3	P2	P3
G3	P2	P3
A1	P2	P4
G1	P2	P4
A2	P2	P4
G2	P2	P4
A3	P2	P4
G3	P2	P4
A1	P2	P1
G1	P2	P1
A2	P2	P1
G2	P2	P1
A3	P2	P1
G3	P2	P1
A1	P2	P2
G1	P2	P2
A2	P2	P2
G2	P2	P2

and wherein the groups P, G and A are as described in "Substituents per Example Libraries 1-14" in the specification.

21 The method of claim 14, wherein the compound is



wherein R4, R2 and R3 are selected from the group combinations of:

R2	R3	R4

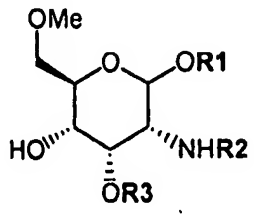
A1	P3	P3
G1	P3	P3
A2	P3	P3
G2	P3	P3
A3	P3	P3
G3	P3	P3
A1	P3	P4
G1	P3	P4
A2	P3	P4
G2	P3	P4
A3	P3	P4
G3	P3	P4
A1	P3	P1
G1	P3	P1
A2	P3	P1
G2	P3	P1
A3	P3	P1
G3	P3	P1
A1	P3	P2
G1	P3	P2
A2	P3	P2
G2	P3	P2
A3	P3	P2
G3	P3	P2
A1	P4	P3
G1	P4	P3
A2	P4	P3
G2	P4	P3
A3	P4	P3
G3	P4	P3
A1	P4	P4
G1	P4	P4
A2	P4	P4
G2	P4	P4
A3	P4	P4
G3	P4	P4
A1	P4	P1
G1	P4	P1
A2	P4	P1
G2	P4	P1
A3	P4	P1
G3	P4	P1
A1	P4	P2
G1	P4	P2
A2	P4	P2
G2	P4	P2

A3	P4	P2
G3	P4	P2
A1	P1	P3
G1	P1	P3
A2	P1	P3
G2	P1	P3
A3	P1	P3
G3	P1	P3
A1	P1	P4
G1	P1	P4
A2	P1	P4
G2	P1	P4
A3	P1	P4
G3	P1	P4
A1	P1	P1
G1	P1	P1
A2	P1	P1
G2	P1	P1
A3	P1	P1
G3	P1	P1
A1	P1	P2
G1	P1	P2
A2	P1	P2
G2	P1	P2
A3	P1	P2
G3	P1	P2
A1	P2	P3
G1	P2	P3
A2	P2	P3
G2	P2	P3
A3	P2	P3
G3	P2	P3
A1	P2	P4
G1	P2	P4
A2	P2	P4
G2	P2	P4
A3	P2	P4
G3	P2	P4
A1	P2	P1
G1	P2	P1
A2	P2	P1
G2	P2	P1
A3	P2	P1
G3	P2	P1
A1	P2	P2
G1	P2	P2

A2	P2	P2
G2	P2	P2

and wherein the groups P, G and A are as described in "Substituents per Example Libraries 1-14" in the specification.

22. The method of claim 15, wherein the compound is



wherein R1, R2 and R3 are selected from the group combinations of:

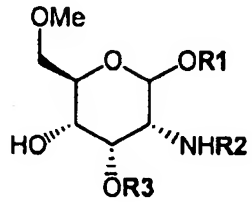
R1	R2	R3
P3	G1	P3
P3	G2	P3
P3	G3	P3
P3	A1	P4
P3	G1	P4
P3	A2	P4
P3	G2	P4
P3	A3	P4
P3	G3	P4
P3	A1	P1
P3	G1	P1
P3	A2	P1
P3	G2	P1
P3	A3	P1
P3	G3	P1
P3	G1	P2
P3	A2	P2
P3	G2	P2
P3	A3	P2
P3	G3	P2
P4	G1	P3
P4	G2	P3
P4	G3	P3

P4	A1	P4
P4	G1	P4
P4	A2	P4
P4	G2	P4
P4	A3	P4
P4	G3	P4
P4	A1	P1
P4	G1	P1
P4	A2	P1
P4	G2	P1
P4	A3	P1
P4	G3	P1
P4	A1	P2
P4	G1	P2
P4	A2	P2
P4	G2	P2
P4	A3	P2
P4	G3	P2
P5	G1	P3
P5	G2	P3
P5	G3	P3
P5	G1	P4
P5	A2	P4
P5	G2	P4
P5	A3	P4
P5	G3	P4
P5	A1	P1
P5	G1	P1
P5	A2	P1
P5	G2	P1
P5	A3	P1
P5	G3	P1
P5	A1	P2
P5	G1	P2
P5	A2	P2
P5	G2	P2
P5	A3	P2
P5	G3	P2
P2	G1	P3
P2	A2	P3
P2	G2	P3
P2	G1	P4
P2	G2	P4
P2	A3	P4
P2	G3	P4
P2	G1	P1

P2	A2	P1
P2	G2	P1
P2	A3	P1
P2	G3	P1
P2	A1	P2
P2	G1	P2
P2	G2	P2
P2	G3	P2

and wherein the groups P, G and A are as described in "Substituents per Example Libraries 1-14" in the specification.

23. The method of claim 14, wherein the compound is



wherein R1, R2 and R3 are selected from the group combinations of:

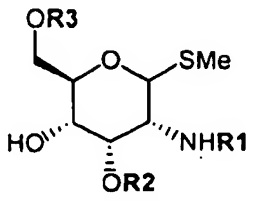
R1	R2	R3
P3	A1	P3
P3	G1	P3
P3	A2	P3
P3	G2	P3
P3	A3	P3
P3	G3	P3
P3	A1	P4
P3	G1	P4
P3	A2	P4
P3	G2	P4
P3	A3	P4
P3	G3	P4
P3	A1	P1
P3	G1	P1
P3	A2	P1
P3	G2	P1

P3	A3	P1
P3	G3	P1
P3	A1	P2
P3	G1	P2
P3	A2	P2
P3	G2	P2
P3	A3	P2
P3	G3	P2
P4	G1	P3
P4	A2	P3
P4	G2	P3
P4	A3	P3
P4	G3	P3
P4	A1	P4
P4	G1	P4
P4	A2	P4
P4	G2	P4
P4	A3	P4
P4	G3	P4
P4	A1	P1
P4	G1	P1
P4	A2	P1
P4	G2	P1
P4	A3	P1
P4	G3	P1
P4	A1	P2
P4	G1	P2
P4	A2	P2
P4	G2	P2
P4	A3	P2
P4	G3	P2
P5	A1	P3
P5	A2	P3
P5	G2	P3
P5	A3	P3
P5	G3	P3
P5	A1	P4
P5	G1	P4
P5	A2	P4
P5	G2	P4
P5	A3	P4
P5	G3	P4
P5	A1	P1
P5	G1	P1
P5	A2	P1
P5	G2	P1

P5	A3	P1
P5	G3	P1
P5	A1	P2
P5	G1	P2
P5	A2	P2
P5	G2	P2
P5	A3	P2
P5	G3	P2
P2	A1	P3
P2	G1	P3
P2	A2	P3
P2	G2	P3
P2	A3	P3
P2	G3	P3
P2	A1	P4
P2	G1	P4
P2	A2	P4
P2	G2	P4
P2	A3	P4
P2	G3	P4
P2	A1	P1
P2	G1	P1
P2	A2	P1
P2	G2	P1
P2	A3	P1
P2	G3	P1
P2	A1	P2
P2	G1	P2
P2	A2	P2
P2	G2	P2
P2	A3	P2
P2	G3	P2

and wherein the groups P, G and A are as described in "Substituents per Example Libraries 1-14" in the specification.

24. The method of claim 15, wherein the compound is

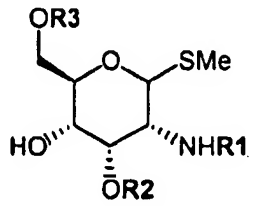


wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
P3	N4	E2
P3	N4	E4
P3	N4	E6
P4	N4	E2
P4	N4	E4

and wherein the groups P, N and E are as described in "Substituents per Example Libraries 1-14" in the specification.

25. The method of claim 14, wherein the compound is

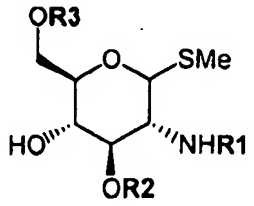


wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
P3	N4	E5
P3	N4	E6
P4	N4	E1
P4	N4	E2
P4	N4	E5

and wherein the groups P, N and E are as described in "Substituents per Example Libraries 1-14" in the specification.

26. The method of claim 15, wherein the compound is

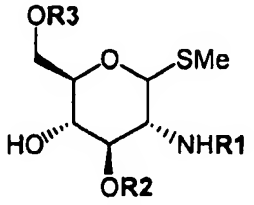


wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
E2	N4	P3
E4	N4	P3
E6	N4	P3
E4	N4	P4
E5	N4	P4
E6	N4	P4

and wherein the groups P, N and E are as described in "Substituents per Example Libraries 1-14" in the specification.

27. The method of claim 14, wherein the compound is



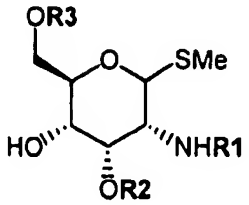
wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
E1	N4	P3
E5	N4	P3
E6	N4	P3
E1	N4	P4
E2	N4	P4
E5	N4	P4

and wherein the groups P, N and E are as described in "Substituents per Example

Libraries 1-14" in the specification.

28. The method of claim 15, wherein the compound is

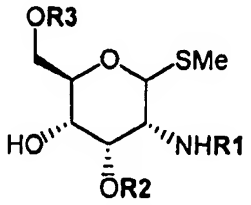


wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
E2	P3	N4
E4	P3	N4
E6	P3	N4
E1	P4	N4
E6	P4	N4

and wherein the groups E, P and N are as described in "Substituents per Example Libraries 1-14" in the specification.

29. The method of claim 14, wherein the compound is

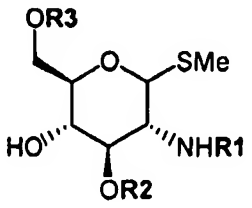


wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
E1	P3	N4
E2	P3	N4
E5	P3	N4
E6	P3	N4
E1	P4	N4

and wherein the groups E, P and N are as described in "Substituents per Example Libraries 1-14" in the specification.

30. The method of claim 15, wherein the compound is

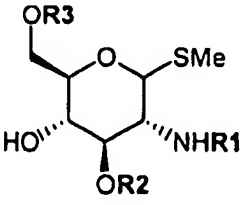


wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
E1	P3	N4
E2	P3	N4
E3	P3	N4
E5	P3	N4
E1	P4	N4
E2	P4	N4
E3	P4	N4
E5	P4	N4

and wherein the groups E, P and N are as described in "Substituents per Example Libraries 1-14" in the specification.

31. The method of claim 14, wherein the compound is

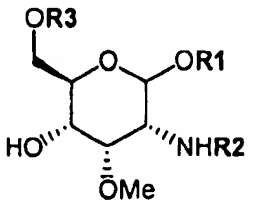


wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
E5	P3	N4
E6	P3	N4
E1	P4	N4
E2	P4	N4
E5	P4	N4

and wherein the groups E, P and N are as described in "Substituents per Example Libraries 1-14" in the specification.

32. The method of claim 15, wherein the compound is

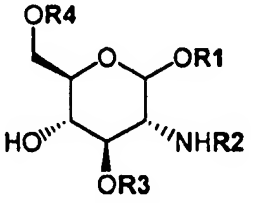


wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
P4	E8	P2
P4	E9	P2
P4	E10	P2
P4	G1	P2
P4	E8	P2
P4	E9	P2
P4	E11	P2
P4	G1	P2

and wherein the groups P, G and E are as described in "Substituents per Example Libraries 1-14" in the specification.

33. The method of claim 15, wherein the compound is



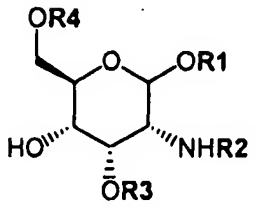
wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4
P2	A2	P4	P2
P2	A2	P4	P2
P2	A2	P4	P3
P2	A2	P4	P3
P2	A2	P4	P4

P2	A2	P4	P4
P2	A2	P2	P2
P2	A2	P2	P2
P2	A2	P2	P3
P2	A2	P2	P4
P2	A2	P2	P4
P2	A2	P3	P2
P2	A2	P3	P3
P2	A2	P3	P3
P2	A2	P3	P4
P2	A3	P4	P2
P2	A3	P4	P2
P2	A3	P4	P4
P2	A3	P4	P4
P2	A3	P2	P2
P2	A3	P2	P4
P2	A3	P2	P4
P2	A3	P3	P2
P2	A3	P3	P2
P2	A3	P3	P3
P2	A3	P3	P4
P4	A2	P4	P3
P4	A2	P4	P4
P4	A2	P2	P2
P4	A2	P2	P3
P4	A2	P2	P3
P4	A2	P2	P4
P4	A2	P2	P4
P4	A2	P3	P2
P4	A2	P3	P3
P4	A2	P3	P4
P4	A3	P4	P2
P4	A3	P4	P3
P4	A3	P4	P4
P4	A3	P2	P2
P4	A3	P2	P2
P4	A3	P2	P3
P4	A3	P2	P3
P4	A3	P2	P4
P4	A3	P2	P4
P4	A3	P3	P2
P4	A3	P3	P4

and wherein the groups P, and A are as described in "Substituents per Example Libraries 1-14" in the specification.

34. The method of claim 15, wherein the compound is

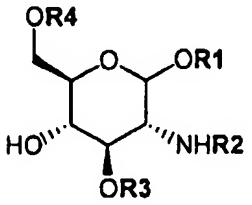


wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4
P3	A2	P4	P2
P3	A2	P4	P3
P3	A2	P4	P4
P3	A2	P2	P2
P3	A2	P2	P3
P3	A2	P2	P4
P3	A2	P3	P2
P3	A2	P3	P3
P3	A2	P3	P4
P3	A3	P4	P2
P3	A3	P4	P4
P3	A3	P2	P2
P3	A3	P2	P3
P3	A3	P2	P4
P3	A3	P3	P2
P3	A3	P3	P4
P2	A2	P4	P2
P2	A2	P4	P3
P2	A2	P4	P4
P2	A2	P2	P2
P2	A2	P2	P3
P2	A2	P2	P4
P2	A2	P3	P2
P2	A2	P3	P3
P2	A2	P3	P4
P2	A3	P4	P2
P2	A3	P4	P3
P2	A3	P4	P4
P2	A3	P2	P2
P2	A3	P2	P3
P2	A3	P2	P4
P2	A3	P3	P2
P2	A3	P3	P3
P2	A3	P3	P4

and wherein the groups P, and A are as described in "Substituents per Example Libraries 1-14" in the specification.

35. The method of claim 15, wherein the compound is

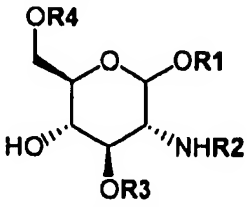


wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4
P3	G1	P4	P2
P3	G1	P4	P2
P3	G1	P4	P3
P3	G1	P4	P3
P3	G1	P4	P4
P3	G1	P2	P2
P3	G1	P2	P2
P3	G1	P2	P3
P3	G1	P2	P4
P3	G1	P2	P4
P3	G1	P1	P2
P3	G1	P1	P3
P3	G1	P1	P3
P3	G1	P1	P4
P3	G1	P1	P4
P3	G2	P4	P2
P3	G2	P4	P2
P3	G2	P4	P3
P3	G2	P4	P3
P3	G2	P4	P4
P3	G2	P4	P4
P3	G2	P2	P2
P3	G2	P2	P3
P3	G2	P2	P3
P3	G2	P2	P4
P3	G2	P2	P4
P3	G2	P1	P2
P3	G2	P1	P2
P3	G2	P1	P3
P3	G2	P1	P4
P3	G2	P1	P4

and wherein the groups P, and A are as described in "Substituents per Example Libraries 1-14" in the specification.

35. The method of claim 15, wherein the compound is



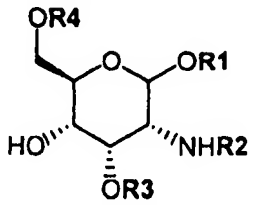
wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4
P3	G1	P4	P2
P3	G1	P4	P2
P3	G1	P4	P3
P3	G1	P4	P3
P3	G1	P4	P4
P3	G1	P2	P2
P3	G1	P2	P2
P3	G1	P2	P3
P3	G1	P2	P4
P3	G1	P2	P4
P3	G1	P1	P2
P3	G1	P1	P3
P3	G1	P1	P3
P3	G1	P1	P4
P3	G1	P1	P4
P3	G2	P4	P2
P3	G2	P4	P2
P3	G2	P4	P3
P3	G2	P4	P3
P3	G2	P4	P4
P3	G2	P4	P4
P3	G2	P2	P2
P3	G2	P2	P3
P3	G2	P2	P3
P3	G2	P2	P4
P3	G2	P2	P4
P3	G2	P1	P2
P3	G2	P1	P2
P3	G2	P1	P3
P3	G2	P1	P4
P3	G2	P1	P4

P3	G2	P1	P5

and wherein the groups P, and G are as described in "Substituents per Example Libraries 1-14" in the specification.

36. The method of claim 15, wherein the compound is



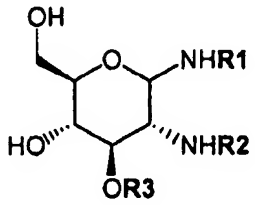
wherein R1, R2, R3 and R4 are selected from the group combinations of:

R1	R2	R3	R4
P1	G1	P4	P2
P1	G1	P4	P3
P1	G1	P4	P4
P1	G1	P2	P3
P1	G1	P2	P4
P1	G1	P1	P3
P1	G1	P1	P4
P1	G2	P4	P2
P1	G2	P4	P3
P1	G2	P4	P4
P1	G2	P2	P2
P1	G2	P2	P3
P1	G2	P2	P4
P1	G2	P1	P2
P1	G2	P1	P3
P1	G2	P1	P4
P4	G1	P4	P2
P4	G1	P4	P3
P4	G1	P4	P4
P4	G1	P2	P2
P4	G1	P2	P3
P4	G1	P2	P4
P4	G1	P1	P2
P4	G1	P1	P3
P4	G1	P1	P4
P4	G2	P4	P2
P4	G2	P4	P3
P4	G2	P4	P4
P4	G2	P2	P2

P4	G2	P2	P3
P4	G2	P2	P4
P4	G2	P1	P2
P4	G2	P1	P3
P4	G2	P1	P4
P1	G3	P3	P3

and wherein the groups P, and G are as described in "Substituents per Example Libraries 1-14" in the specification.

37. The method of claim 15, wherein the compound is



wherein R1, R2 and R3 are selected from the group combinations of:

R1	R2	R3
A2	G4	P3
A2	G4	P12
A2	G4	P13
A2	G4	P1
A2	E1	P3
A2	E1	P4
A2	E1	P12
A2	E1	P13
A1	E1	P3
A1	E1	P4

and wherein the groups P, A and E are as described in "Substituents per Example Libraries 1-14" in the specification.

38. A pharmaceutical formulation comprising a compound as claimed in claim 1 or a pharmaceutically acceptable salt thereof, together with one or more pharmaceutically acceptable carriers, diluents or excipients.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2003/001347

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. [7]: A61K 31/7008, 31/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPAT, CAPLUS; keywords- GPCR, G-Protein Coupled Receptor, amino sugars, inhibit, agonist, antagonist.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Budavari, S et al, "THE MERCK INDEX" Thirteenth Edition; pages 793-794, monograph 4471.	38
A	WO 1999/00406 A (The University of Queensland) 7 January 1999 (07.01.99) See whole document.	1-38
A	WO 2001/98270 A (DuPont Pharmaceuticals Company) 27 December 2001 (21.12.01). See whole document.	1-38

☐ Further documents are listed in the continuation of Box C ☒ See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
8 January 2004

Date of mailing of the international search report
15 JAN 2004

Name and mailing address of the ISA/AU

AUSTRALIAN PATENT OFFICE
PO BOX 200, WODEN ACT 2606, AUSTRALIA
E-mail address: pct@ipaustralia.gov.au
Facsimile No. (02) 6285 3929

Authorized officer

G.R.PETERS

Telephone No : (02) 6283 2184

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU2003/001347

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
WO	1999/00406	AU	80926/98	EP	1017713		
WO	2001/98270	AU	19406/00	AU	20572/00	BR	9917038
		CA	23446933	EP	1140087	EP	1158980
		NO	20012977	US	6605623		

END OF ANNEX